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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/564,193 | 01/06/2006 | Johannes Hubertus Wieringa | 2003.796US | 7506 |
| 67706 7590 03/25/2008 ORGANON USA, INC. PATENT DEPARTMENT 56 LIVINGSTON AVENUE ROSELAND, NJ 07068 | | | | |
| EXAMINER JARRELL, NOBLE E | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1624 | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/564,193

Applicant(s)

WIERINGA ET AL.

Examiner

Noble Jarrell

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SE-US)
Paper No(s)/Mail Date 4/26/06/5/26/06
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I in the reply filed on 2/7/08 is acknowledged. The traversal is on the ground(s) that a serious burden to search both groups has not been established. This is not found persuasive because claim 10 is focused on the selection of an acid or acid/solvent system, rather than the preparation of mirtazapine. Since the foci of the two groups is different, a search burden does exist.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
3. Claims 3, 7, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What "protic acid derivative" is referred to? A protic acid derivative includes ester, amide, and any carboxylic acid derivative, because formic acid is considered a protic acid. Because claim 9 depends on claim 7, it is rejected as well.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Van der Burg (US 4,062,848, issued December 13, 1977, cited in IDS). Van der Burg teaches example I, in column 11, lines 10-26. This example teaches the rings closing of reaction of a compound of

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formula I where variable X is OH to mirtazapine in the presence of concentrated sulfuric acid. In further support of this, example XIX (column 20, lines 5-35) teach enantiomeric resolution of mirtazapine. Example XIX also teaches the mixing of tartaric acid (an organic acid) in ethanol (a polar protic organic solvent) in the purification of mirtazapine. After this step, the product is washed with ammonia and extracted with diethyl ether, evaporated, and crystallized with petroleum ether. Thus, claims 1-3 and 6 are anticipated. Claim 4 is anticipated because Van der Burg suggest that polyphosphoric acid can also be used (column 1, line 59-column 2, line 10). Claim 5 is anticipated due to teachings from *in re Aller* (105 USPQ 233). *In re Aller* teaches:

Normally, change in temperature, concentration, or both, is not patentable modification; however, such changes may impart patentability to process if ranges claimed produce new and unexpected result which is different in kind and not merely in degree from results of prior art; such ranges are termed "critical" ranges, and applicant has burden of proving such criticality; even though applicant's modification results in great improvement and utility over prior art, it may still not be patentable if modification was within capabilities of one skilled in art; more particularly, where general conditions of claim are disclosed in prior art, it is not inventive to discover optimum or workable ranges by routine experimentation.

Thus claims 1-5 are anticipated by Van der Burg. It is noted that WO 00/62782 (cited in IDS) is also considered prior art for these claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over van der Burg (same reference as the 102(b) rejection). Van der Burg teaches the enantiomeric resolution of mirtazapine in example XIX. Van der Burg does not teach the use of an mineral acid in combination with a polar coordinating solvent. However, van der Burg does teach the use of O,O-dibenzoyltartaric acid in combination with ethanol. However, the use of an organic acid in place would have been obvious because "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success it is likely the product not of innovation but of ordinary skill and common sense." It would be obvious to one of ordinary skill in the art to try an organic acid in place of a mineral acid. In the instant case tartaric acid has a pK_a of 2.98 (considered a strong acid) ("Dissociation Constants of Organic Acids and Bases", <http://www.zirchrom.com/organic.htm>, accessed March 17, 2008). One would not expect a dibenzoylated version of tartaric acid to be a much weaker acid than unmodified tartaric acid, because the internal hydroxyl groups are esterified, not the terminal carboxylic acid groups. March (*Advanced Organic Chemistry, Fourth Edition*, 1992, pages 250-252) teaches that the pK_a of mineral acids such as HF, HONO, H_2CO_3 , and H_2S are 3.29, 3.29, 6.35, and 7.00, respectively. As it has been shown, the pK_a of tartaric acid is 2.98, and is a stronger acid than any of these mineral acids. As a result of this analysis, it would be obvious to one of ordinary skill in the art to replace a mineral acid with O, O-dibenzoyltartaric acid.

Conclusion

9. No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

**/James O. Wilson/
Supervisory Patent Examiner
Art Unit 1624**